REMARKS

Formal Matters

Claims 3-10, 14-23 and 29-32 were examined and stand rejected.

Claims 6, 8-10, 23, 29-32 and 35-39 are pending after entry of the amendments set forth herein.

Applicants respectfully request reconsideration of the application in view of the amendments and remarks made herein.

Support for the amendments to claims 6, 8-10, 23, 29-32 and new claims 35-39 can be found throughout the specification, at, for example, page 3, line 18; page 17, lines 4-6; page 56, lines 7-10; page 57, lines 7-9 and lines 23-24. As such, no new matter has been added.

Drawings

Figure 2A has been corrected in accordance with the Notice to Comply With Requirements for Patent Applications Containing Nucleotide Sequence and/or Amino Acid Sequence Disclosures which form had accompanied the Office Action. In particular, Figure 2A has been labeled "SEQ ID NO: 1." The amendment to Figure 2A merely adds a sequence identifier to the figure and does not introduce new matter. Entry of the foregoing amendment is respectfully requested.

Sequence Compliance

The Examiner has noted that the instant application allegedly fails to comply with the requirements of 37 CFR 1.821 through 1.825, in particular because the sequence disclosed in Figure 2A lacks a sequence identifier

Applicants submit herewith a replacement copy of Figure 2A which is identified as SEQ ID NO: 1. The content of the replacement copy and computer readable copies of

the sequence previously submitted in this application are the same. As this sequence was already included in the submitted Sequence Listing (SEQ ID NO:1), Applicants believe that no substitute Sequence Listing is required, and that Applicants are in full compliance with the requirements of 37 CFR 1.821 through 1.825.

Accordingly, Applicants respectfully request entry of the paper and computer readable forms of the sequence listing into the application.

Specification

The specification was objected to because the Office Action asserted the following informalities: "the sentence bridging lines 19-21 on page 1 is incomplete." (Office Action, page 7) The Applicants replaced the first paragraph on page one, line 10 of the present application with the first paragraph of page one of U.S. Provisional Application 60/311,056, filed August 8, 2001 the entire contents of which is incorporated by reference in the present application. As such, no new matter has been introduced into the application. Thus, applicants submit that the informalities are overcome in view of this amendment.

Rejection under 35 U.S.C. § 112, 1st paragraph.

Claims 3-10, 14-23 and 29-32 stand rejected under 35 U.S.C. § 112, 1st paragraph. Claims 4-5, 7 and 14-22 have been canceled. As such, the rejection with respect to these now-canceled claims is moot.

With respect to the pending claims, including new claims 35-39, it is asserted in the Office Action that the specification does not provide an adequate written description for or enable the claimed invention for any and all FPR-RS4 genes other than FPR-RS4 gene encompassed by SEQ ID NO: 1. (Office Action, page 8)

Specifically, the Office Action asserts that the specification, while being enabling for a knockout mouse with a homozygous disruption in a FPR-RS4 gene identified as SEQ ID NO: 1 wherein said mouse exhibits increased anxiety, or deficits in motor coordination, balance, ataxia or decreased susceptibility to seizure, a method of making said mouse by introducing a knockout construct into an embryonic stem cell, does not

reasonably provide enablement or adequate written support for a transgenic mouse comprising **any type** of disrupted FPR-RS4 gene having **any phenotype** other that increased anxiety, or deficits in motor coordination, balance, ataxia or decreased susceptibility to seizure and a method of making the knockout mouse by introducing a knockout construct into **any type** of cell.

In connection with this rejection, the Examiner states that "limiting claims 3-6 and 10 to a transgenic mouse or mouse cell and deleting 'a' preceding 'FPR-RS4' in claims 3, 4, 6, 9, 10, 14, 15, 17, 20 and 23 would overcome this rejection." Further, the Examiner states "the claims should be limited to a homozygous disruption of the FPR-RS4 gene." Applicants have adopted Examiner's suggested modifications, or addressed Examiner's rejection, by: (1) limiting the above-mentioned claims to a transgenic mouse or mouse cell and deleting 'a' preceding FPR-RS4; (2) inserting homozygous to describe the type of disruption in the FPR-RS4 gene; (3) reciting the specific type of cell (i.e., mouse ES cell) into which the knockout targeting construct is introduced; and (4) inserting phenotypic language into the pending amended claims such that the transgenic mouse having a homozygous disruption in FPR-RS4 exhibits increased anxiety, or deficits in motor coordination, balance or ataxia or decreased susceptibility to seizure.

In light of the foregoing, Applicants submit that the rejections of the above-cited claims under 35 U.S.C. § 112, first paragraph, both as to enablement and written description, are overcome in view of the amendments, claim cancellations, and remarks set forth herein. The Examiner is thus respectfully requested to withdraw these rejections.

Rejection under 35 U.S.C. § 103(a).

Claims 3-9 and 14 stand rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Capecchi (Scientific American, 1994, vol. 270, pp 34-41) in view of Gao (1998, Genomics, Vol. 51, pages 270-276). Applicants respectfully traverse this rejection. However, in view of the cancellation of claims 4-5, 7 and 14 and in view of the amendments to the pending claims, Applicants submit that the rejection under 35 U.S.C. § 103 is no longer relevant.

In order to establish a *prima facie* case of obviousness, the Examiner must meet three basic criteria: there must be some suggestion or motivation to modify a primary reference or combine reference teachings; there must be a reasonable expectation of success; and the prior art reference(s) **must teach or suggest all the claim limitations**. See MPEP §2143.

According to the Examiner, Capecchi discloses transforming a cell with a nucleic acid construct comprising a disruption in the *Hox*A-3 gene, resulting in an inactivating insertion of a selective marker gene into the endogenous *Hox*A-3 locus, and using said cell to generate a mouse whose genome comprises a disruption in the *Hox*A-3 gene. Capecchi very generally discusses the method of targeted gene replacement, specifically as it relates to disrupting the *Hox*A-3 gene. Capecchi then further specifically discusses the effect or phenotype of a knockout of the *Hox*A-3 gene in mice observed in his laboratory, which revealed a role for *Hox*A-3 in development of the mouse embryo.

Gao, as characterized by the Examiner, teaches the cloning and characterization of the mouse FPR-RS4 gene. The Examiner relies on the teachings of Gao to provide motivation to disrupt the FPR-RS4 gene.

However, neither Capecchi nor Gao, alone or in combination, teaches all of the limitations as presently claimed. As acknowledged by the Examiner, Capecchi provides no disclosure or teaching of how to make a FPR-RS4 gene knockout mouse. More particularly, Capecchi does not disclose a transgenic mouse comprising a disruption in a FPR-RS4 gene, wherein the transgenic mouse exhibits a specific phenotype, particularly a phenotype of a increased anxiety, or deficits in motor coordination, balance or ataxia or decreased susceptibility to seizure, as presently claimed. Likewise, Gao does not provide any teaching or suggestion relating to targeted disruptions in any gene, particularly in a FPR-RS4 gene. More particularly, the disclosure of Gao fails to provide any teaching or suggestion that relates to transgenic mice or cells, and in particular to those transgenic mice and cells as recited in the pending claims.

Taken together, the disclosures of Capecchi and Gao are devoid of any teaching or suggestion of disrupting the FPR-RS4 gene, and in particular, are deficient of any teachings or suggestions of the transgenic mice and cells as recited in the pending claims.

More particularly, the disclosures of Capecchi and Gao, alone or combined, do not teach or suggest in any way transgenic mice comprising disrupted FPR-RS4 genes, wherein such transgenic mice exhibit a phenotype, and in particular exhibit a phenotype of a increased anxiety, or deficits in motor coordination, balance or ataxia or decreased susceptibility to seizure as claimed by the present invention.

The references, either alone or combined as suggested by the Examiner, fail to make obvious the claimed invention "absent any phenotypic requirements for the claimed transgenic mouse." As amended, the claims describe phenotypic abnormalities for the transgenic mice including increased anxiety, or deficits in motor coordination, balance or ataxia or decreased susceptibility to seizure.

As the obviousness rejection is no longer relevant as result of the cancellation of claims 4-5, 7 and 14, amended claims 3, 6, 8-9 and new claims 35-39 are not obvious in view of the teachings of Capecchi and Gao, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103.

Claims 3-10 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Beach (1999, USPN 5,919,997) in view of Gao (1998, Genomics, Vol. 51, pages 270-276). Applicants respectfully traverse this rejection. However, in view of the cancellation of claims 3-5, 7 and 14 and in view of the amendments to the pending claims, Applicants submit that the rejection under 35 U.S.C. § 103 is no longer relevant.

In order to establish a *prima facie* case of obviousness, the Examiner must meet three basic criteria: there must be some suggestion or motivation to modify a primary reference or combine reference teachings; there must be a reasonable expectation of success; and the prior art reference(s) **must teach or suggest all the claim limitations**. See MPEP §2143.

As amended, the claims describe phenotypic abnormalities for the transgenic mice including increased anxiety, or deficits in motor coordination, balance or ataxia or decreased susceptibility to seizure.

According to the Examiner, Beach discloses transforming a cell with a nucleic acid construct comprising a disruption in the INK4 gene, resulting in an inactivating

insertion of a selective marker gene into the endogenous INK4 locus, and using said cell to generate a knockout mouse whose genome comprises a disruption in the INK4 gene. According to the Examiner, Beach discloses administering compounds to the transgenic knockout mice comprising a disruption in the INK4 gene to screen for agents that affect the INK4 mutant phenotype and modulate expression or function of INK4.

Gao, as characterized by the Examiner, teaches the cloning and characterization of the mouse FPR-RS4 gene. The Examiner relies on the teachings of Gao to provide motivation to disrupt the FPR-RS4 gene.

However, neither Beach nor Gao, alone or in combination, teaches all of the limitations as presently claimed. In particular, Beach does not disclose a transgenic mouse comprising a disruption in a FPR-RS4 gene, wherein the transgenic mouse exhibits a specific phenotype, particularly a phenotype of a increased anxiety, or deficits in motor coordination, balance or ataxia or decreased susceptibility to seizure, as presently claimed. Likewise, Gao does not provide any teaching or suggestion relating to targeted disruptions in any gene, particularly in a FPR-RS4 gene. More particularly, the disclosure of Gao fails to provide any teaching or suggestion that relates to transgenic mice or cells, and in particular to those transgenic mice and cells as recited in the pending claims.

Taken together, the disclosures of Beach and Gao are devoid of any teaching or suggestion of disrupting the FPR-RS4 gene, and in particular, are deficient of any teachings or suggestions of the transgenic mice and cells as recited in the pending claims. More particularly, the disclosures of Beach and Gao, alone or combined, do not teach or suggest in any way transgenic mice comprising disrupted FPR-RS4 genes, wherein such transgenic mice exhibit a phenotype, and in particular exhibit a phenotype of a increased anxiety, or deficits in motor coordination, balance or ataxia or decreased susceptibility to seizure as claimed by the present invention.

As the obviousness rejection is no longer relevant as result of the cancellation of claims 3-5, 7 and 14, amended claims 6, 8-9 and new claims 35-39 are not obvious in view of the teachings of Beacg and Gao, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103.

Conclusion.

Applicants submit that all of the pending claims are in condition for allowance, which action is requested. If the Examiner finds that a telephone conference would expedite the prosecution of this application, please telephone the undersigned at the number provided.

The Commissioner is hereby authorized to charge any underpayment of fees associated with this communication, including any necessary fees for extensions of time, or credit any overpayment to Deposit Account No. 50-1271.

Respectfully submitted,
DELTAGEN, INC.

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By: Nicole A. Verona
Nicole A. Verona
Registration No. 47,153

DELTAGEN, INC.
700 Bay Road
Redwood City, CA 94063
Telephone: (650) 569-5100
Facsimile: (650) 569-5280